```
=> gene (s) gun
L1         1466 GENE (S) GUN

=> HSV and L1
L2            5 HSV AND L1

=> vector and L1
L3          445 VECTOR AND L1

=> "25 kilobase"
L4          297 "25 KILOBASE"

=> L1 and L4
L5            0 L1 AND L4

=> "5 kilobase"
L6         3997 "5 KILOBASE"

=> L1 and L6
L7            0 L1 AND L6

=> HIV and L1
L8           70 HIV AND L1

=> adenovirus and l1
L9           41 ADENOVIRUS AND L1

=> "viral vector"
L10       13167 "VIRAL VECTOR"

=> L10 and L8
L11           8 L10 AND L8

=> L10 and L9
L12          13 L10 AND L9

=> HBV and L10
L13          44 HBV AND L10

=> L13 and l1
L14           0 L13 AND L1

=> HBV and l1
L15          14 HBV AND L1

=> PHV and L10
L16           0 PHV AND L10

=> DNA (w) vaccine
L17        6153 DNA (W) VACCINE

=> L1 and L17
L18         407 L1 AND L17

=> HCV and L18
L19           3 HCV AND L18

=> HBV and L18
L20           5 HBV AND L18

=> HIV and L17
L21         780 HIV AND L17

=> L1 and L21
L22          27 L1 AND L21

=> cosmid
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updated search 06/08/2005 BDL

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L23      12065 COSMID

=> L23 and L17
L24          3 L23 AND L17

=> L23 and L1
L25          4 L23 AND L1

=> gold and l1
L26        200 GOLD AND L1

=> L26 and L15
L27          1 L26 AND L15

=> L26 and L12
L28          0 L26 AND L12

=> L26 and L11
L29          5 L26 AND L11

=> L26 and L2
L30          0 L26 AND L2

=> L26 and L19
L31          0 L26 AND L19

=> L26 and L20
L32          0 L26 AND L20

=> L26 and L22
L33          1 L26 AND L22

=> L26 and L24
L34          0 L26 AND L24

=> L26 and L25
L35          0 L26 AND L25

=> D L27 IBIB ABS
```

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:788681 CAPLUS
DOCUMENT NUMBER: 130:51331
TITLE: Preparation and use of **viral vectors** for mixed envelope protein immunogenic composition against human immunodeficiency viruses
INVENTOR(S): Hurwitz, Julia; Slobod, Karen
PATENT ASSIGNEE(S): St. Jude Children's Research Hospital, USA
SOURCE: U.S., 36 pp., Cont.-in-part of U.S. 5,741,492.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5846546	A	19981208	US 1997-788815	19970123
US 5741492	A	19980421	US 1996-590288	19960123
CA 2243570	AA	19970731	CA 1997-2243570	19970123
CA 2243570	C	20010814		
CN 1214083	A	19990414	CN 1997-193234	19970123
EP 1378516	A1	20040107	EP 2003-77363	19970123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, AL				
US 6086891	A	20000711	US 1998-157963	19980921
US 6723558	B1	20040420	US 2000-568105	20000510

PRIORITY APPLN. INFO.:

US 1996-590288	A2	19960123
US 1997-788815	A3	19970123
EP 1997-903823	A3	19970731
US 1998-157963	A1	19980921

AB Polyenv immunogenic composition are provided that comprise mixts. of at least 4 different recombinant viruses that each express a different **HIV** env variant or a portion thereof containing both constant and variable regions, as well as methods of making and using such polyenv immunogenic composition and viruses. The immunogenic composition of the invention are optimally combined with a recombinant **HIV** env booster, or a recombinant **HIV** env gene DNA priming or boosting vaccine.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:305212 CAPLUS
DOCUMENT NUMBER: 126:338815
TITLE: Topical application of viral vectors for epidermal gene transfer
AUTHOR(S): Lu, Bo; Federoff, Howard J.; Wang, Yibin; Goldsmith, Lowell A.; Scott, Glynis
CORPORATE SOURCE: Departments Dermatol. Neurol., Univ. Rochester Sch. Med. Dentistry, Rochester, NY, USA
SOURCE: Journal of Investigative Dermatology (1997), 108(5), 803-808
CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Efficient gene transfer with extended gene expression is essential for successful treatment of skin diseases using gene therapy. Previously we evaluated a phys. **gene** transfer method (**gene gun** delivery) for its ability to transfer the epidermis in vivo. In this study, we tested two viral vectors for their ability to transduce murine epidermis through topical application. Both an adenoviral vector and a herpes simplex virus (**HSV**) amplicon vector transduced murine epidermis with high efficiency after topical application. Differences in amount and duration of transgene expression were compared between these two vectors. Quant. anal. of reporter lacZ **gene** expression showed that the viral vector-mediated **gene** transfers were superior to **gene-gun** delivery of plasmid DNA. Significant necrosis and cytotoxicity, however, were observed in the **HSV**-treated skin. In addition, we show that murine epidermis developed hyperkeratosis and acanthosis 4 d after an adenoviral vector containing a human TGF-α expression unit was applied topically. Finally we demonstrate the feasibility of transduction of fetal skin in utero by intraamniotic injection of an adenovirus vector.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 25 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:454559 BIOSIS
DOCUMENT NUMBER: PREV199799753762
TITLE: Manipulation of **HIV**-1 gp120-specific immune responses elicited via **gene gun**-based DNA immunization.
AUTHOR(S): Prayaga, Sudhirdas K.; Ford, Maura J.; Haynes, Joel R. [Reprint author]
CORPORATE SOURCE: Heska Corp., 1825 Sharp Point Dr., Fort Collins, CO 80525, USA
SOURCE: Vaccine, (1997) Vol. 15, No. 12-13, pp. 1349-1352. CODEN: VACCDE. ISSN: 0264-410X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Oct 1997
Last Updated on STN: 27 Oct 1997

AB **Gene gun**-based DNA immunization using vectors encoding **HIV**-1 gp120 or influenza virus nucleoprotein result in Th2-like immune responses following successive immunizations. The codelivery of vectors encoding IL-2, IL-7, or IL-12 blocked this effect by markedly enhancing gp120-specific interferon gamma production, and suppressing IL-4 and IgG1 responses. An unbiased augmentation of all immune responses was observed by increasing the resting period between immunizations. In this case, IFN-gamma production following in vitro stimulation increased by over 1000-fold, while IL-4, IgG1, and IgG2a responses were elevated as well. Interestingly, cytokine gene codelivery, in the context of the longer resting period, provided no additional stimulation of Th1-like responses such as IFN-gamma and IgG2a production, although there was still some suppression of IL-4 production. These data demonstrate that the quality and magnitude of responses elicited following epidermal administration of **DNA vaccines** can be manipulated by multiple means.

L22 ANSWER 26 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:366986 BIOSIS
DOCUMENT NUMBER: PREV199799658919
TITLE: Enhancement of immunodeficiency virus-specific immune responses in DNA-immunized rhesus macaques.
AUTHOR(S): Fuller, Deborah H. [Reprint author]; Corb, Michael Murphey; Barnett, Susan; Steimer, Kathelyn; Haynes, Joel R. [Reprint author]
CORPORATE SOURCE: Auragen Inc., Middleton, WI, USA
SOURCE: Vaccine, (1997) Vol. 15, No. 8, pp. 924-926. CODEN: VACCDE. ISSN: 0264-410X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Aug 1997
Last Updated on STN: 25 Aug 1997

AB In contrast to results obtained with plasmid DNA vectors encoding antigens from viruses such as influenza and hepatitis B, plasmids coding for antigens from primate immunodeficiency viruses have elicited relatively weak antibody responses following **gene gun**-mediated DNA immunization of rhesus monkeys. In an effort to augment these responses, the importance of the immunization schedule was investigated, as well as the possible synergy that might result from boosting **gene gun**-primed animals with other routes of immunization. Here we demonstrate that endpoint gp120-specific antibody titers can be enhanced as much as tenfold by reducing the number of immunizations and lengthening the resting period between immunizations. In addition, boosting **gene gun**-primed animals with either recombinant subunits or gp120-expressing vaccinia recombinants resulted in synergistic responses.

TITLE: Immune responses but no protection against SHIV by **gene-gun** delivery of **HIV**-1 DNA followed by recombinant subunit protein boosts.
AUTHOR(S): Putkonen, Per [Reprint author]; Quesada-Rolander, Marlene; Leandersson, Ann-Charlotte; Schwartz, Stefan; Thorstensson, Rigmor; Okuda, Kenji; Wahren, Britta; Hinkula, Jorma
CORPORATE SOURCE: Swedish Inst. Infectious Dis. Control, Microbiol Tumorbiol Cent., Karolinska Inst., S-105 21 Stockholm, Sweden
SOURCE: Virology, (Oct. 25, 1998) Vol. 250, No. 2, pp. 293-301. print.
CODEN: VIRLAX. ISSN: 0042-6822.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Dec 1998
Last Updated on STN: 18 Dec 1998

AB The efficacy of combining immunization with human immunodeficiency vitus type 1 (**HIV**-1) DNA and **HIV**-1 recombinant proteins to obtain protection from chimeric simian/human immunodeficiency virus (SHIV) was determined. Four cynomolgus monkeys received four **gene-gun** immunizations intraepidermally of plasmid DNA encoding **HIV**-1 LAI env (gp160), gag, tat, nef, and rev proteins. Ten micrograms of DNA was used per immunization. The animals were boosted twice intramuscularly with 50 mug of **HIV**-1LAI Env (MicroGeneSys), Gag, Tat, Nef, and Rev recombinant proteins mixed in Ribi adjuvant. The antibody responses were amplified following the administration of the recombinant subunit boosts. One month after the final subunit immunization, the vaccinated animals-together with four control animals were challenged intravenously with 10 monkey infectious doses of SHIV that expresses the env, tat and rev genes of **HIV**-1 and gag and nef from SIV. However, only low titers of neutralizing antibodies were present at the day of challenge. The consecutive **HIV**-1 DNA and recombinant protein immunizations induced B- and T-cell responses but not protection against SHIV replication nor reduction of the viral load.

L22 ANSWER 24 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:257620 BIOSIS
DOCUMENT NUMBER: PREV199800257620
TITLE: Improved humoral and cellular immune responses against the gp120 V3 loop of **HIV**-1 following genetic immunization with a chimeric **DNA vaccine** encoding the V3 inserted into the hepatitis B surface antigen.
AUTHOR(S): Fomsgaard,a., H. V. Nielsen [Reprint author]; Bryder, K.; Nielsen, C.; Machuca, R.; Bruun, L.; Hansen, J.; Buus, S.
CORPORATE SOURCE: Dep. Virol., Statens Serum Inst., 5 Artillerivej DK-2300 Copenhagen S, Denmark
SOURCE: Scandinavian Journal of Immunology, (April, 1998) Vol. 47, No. 4, pp. 289-295. print.
CODEN: SJIMAX. ISSN: 0300-9475.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 1998
Last Updated on STN: 9 Jun 1998

AB The gp120-derived V3 loop of **HIV**-1 is involved in co-receptor interaction, it guides cell tropism, and contains an epitope for antibody neutralization. Thus, **HIV**-1 V3 is an attractive vaccine candidate. The V3 of the MN strain (MN V3) contains both B- and T-cell epitopes, including a known mouse H-2d-restricted cytotoxic T lymphocyte (CTL) epitope. In an attempt to improve the immunogenicity of V3 in **DNA vaccines**, a plasmid expressing MN V3 as a fusion protein with the highly immunogenic middle (pre-S2+S) surface antigen of hepatitis B virus (HBsAg) was constructed. Epidermal inoculation by **gene gun** was used for genetic immunization in a mouse model. Antibody and CTL responses to MN V3 and HBsAg were measured and compared with the immune responses obtained after vaccination with plasmids encoding the complete **HIV**-1 MN gp160 and HBsAg

(pre-S2+S), respectively. DNA vaccination with the **HIV** MN gp160 envelope plasmid induced a slow and low titred anti-MN V3 antibody response at 12 weeks post-inoculation (p.i.) and a late appearing (7 weeks), weak and variable CTL response. In contrast, DNA vaccination with the HBsAg-encoding plasmid induced a rapid and high titred anti-HBsAg antibody response and a uniform strong anti-HBs CTL response already 1 week p.i. in all mice. DNA vaccination with the chimeric MN V3/HBsAg plasmid elicited humoral responses against both viruses within 3-6 weeks which peaked at 6-12 weeks and remained stable for at least 25 weeks. In addition, specific CTL responses were induced in all mice against both MN V3 and HBsAg already within the first 3 weeks, lasting at least II weeks. Thus, HBsAg acts as a 'genetic vaccine adjuvant' augmenting and accelerating the cellular and humoral immune response against the inserted MN V3 loop. Such chimeric **HIV**-HBsAg plasmid constructs may be useful in DNA immunizations as a 'carrier' of protein regions or minimal epitopes which are less exposed or poorly immunogenic.

ACCESSION NUMBER: 1999:195880 BIOSIS
DOCUMENT NUMBER: PREV199900195880
TITLE: **HIV**-1 **DNA vaccines**.
AUTHOR(S): Fomsgaard, Anders [Reprint author]
CORPORATE SOURCE: Department of Virology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S, Denmark
SOURCE: Immunology Letters, (Jan., 1999) Vol. 65, No. 1-2, pp. 127-131. print.
CODEN: IMLED6. ISSN: 0165-2478.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 May 1999
Last Updated on STN: 25 May 1999

AB **HIV**-1 was among the original **DNA vaccine** targets and **HIV DNA vaccines** are now in human trials. Lack of strong correlates of protective immunity makes vaccine design difficult; however, **DNA vaccines** have the potential to be an ideal vaccine and therapeutic approach against **HIV**-1. **DNA vaccines** induce conformational -dependent antibodies, mimic live vaccines but without the pathogenic potential, and can easily be made polyvalent. Genes which encode important CTL and antibody epitopes can be included while those that confer pathogenicity, virulence, antibody enhancement or represent non-conserved epitopes can be excluded. In our hands pre-treatment of muscles with bupivacaine or cardiotoxin did not offer any advantage over no muscle pre-treatment or **gene gun** inoculation of skin although **gene gun** immunization seem to favour a Th2 type response. As **DNA vaccine** candidates we have compared vaccines encoding native **HIV** MN gp160 with Rev-independent synthetic genes encoding MNgp160 and MNgp120 using mammalian high expression codons. In these experiments the gene encoding secreted gp120 gave highest antibody neutralizing titers. High and fast antibody responses could also be obtained by transferring the **HIV** -1 MN V3 loop to the secreted HBsAg as a fusion gene vaccine. Thus, in the case of **HIV**-1 MN genes encoding secreted surface glycoproteins may be preferred instead of membrane bound envelopes. CTL responses were induced in all cases. However, in order to meet the high diversity of **HIV** and HLA types our approach is to include many CTL epitopes in a multivalent minigene vaccine. We found that **gene gun** DNA vaccination with minimal epitopes could induce specific CTL. Flanking sequences influenced the CTL response but was not needed. **DNA vaccines** encoding known and computer predicted CTL epitopes are now being developed.

L22 ANSWER 20 OF 27 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:216837 BIOSIS
DOCUMENT NUMBER: PREV199900216837
TITLE: Induction of mucosal IgA by a novel jet delivery technique for **HIV**-1 DNA.
AUTHOR(S): Lundholm, Peter [Reprint author]; Asakura, Yusuke; Hinkula, Jorma; Lucht, Erik; Wahren, Britta
CORPORATE SOURCE: Swedish Institute for Infectious Disease Control, Microbiology and Tumorbiology Center, Karolinska Institute, 171 82, Stockholm, Sweden
SOURCE: Vaccine, (April 9, 1999) Vol. 17, No. 15-16, pp. 2036-2042. print.
CODEN: VACCDE. ISSN: 0264-410X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 May 1999
Last Updated on STN: 26 May 1999

AB Novel ways of delivering plasmid DNA to elicit humoral IgA, IgG and cell-mediated immune responses in mice were investigated. Intraoral administration of DNA in the cheek, using a jet immunization technique, elicited the highest IgA mucosal responses. Intranasal immunization gave strong mucosal IgA responses and persistent systemic IgG. Immunoglobulin isotype analysis revealed an IgG1 profile for intramuscular tongue and **gene gun** immunizations and an IgG2a profile following oral jet injection and intranasal application. The route of delivery was of importance for the characteristics and quality of the mucosal immune response following DNA immunization. For **DNA vaccine** delivery, the intraoral jet injection technique has the advantages of being a simple and rapid way of administering the DNA in solution and of provoking specific mucosal IgA when administered in the mucosal associated lymphoid tissue.

L22 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:426180 CAPLUS
DOCUMENT NUMBER: 129:201753
TITLE: **DNA vaccines**: a review of developments
AUTHOR(S): Webster, Robert G.; Robinson, Harriet L.
CORPORATE SOURCE: Department of Virology and Molecular Biology, St. Jude Children's Research Hospital, Memphis, TN, USA
SOURCE: BioDrugs (1997), 8(4), 273-292
CODEN: BIDRF4; ISSN: 1173-8804
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 110 refs. Immunization with purified DNA is a powerful technique for inducing immune responses. The concept is very simple, involving insertion of the gene encoding the antigen of choice into a bacterial plasmid, and injection of the plasmid into the host where the antigen is expressed and induces humoral and cellular immunity. This technol. can induce immunity to all antigens that can be encoded by DNA; this includes all protein, but not carbohydrate, antigens. DNA immunization appears to result in presentation of antigens to the host's immune system in a natural form, similar to that achieved with live attenuated vaccines. The most efficacious routes for DNA immunization are bombardment with particles coated with DNA (**gene-gun**), followed by i.m. and intradermal administration. The efficiency of transfection of host cells is low, but sufficient to induce immunol. responsiveness. The DNA plasmid is retained in the transfected cells in an unintegrated form for the life of the cell. The majority of transfected cells are eliminated, but residual expression has been detected for longer periods. In animal model systems, DNA immunization has been shown to induce protective immunity to influenza, herpes, rabies, hepatitis B and lymphocytic choriomeningitis viruses, and to malaria and mycobacteria. However, strategies to induce protective immunity to **HIV** and other disease agents remain to be developed. **DNA vaccines** permit modulation of the immune response by altering the route or method of DNA administration, by including immunostimulatory sequences in the plasmid, and by co-administration of cytokine genes with the gene encoding the antigen of interest. A T helper 1 response provides cell-mediated immune killing of infected cells and neutralizing antibody production, while a T helper 2 response induces IgE and allergic responses. The advantages of DNA immunization are: (i) similarity to live attenuated vaccination but without the possibility of contamination with undesirable agents; (ii) correct presentation of antigen; (iii) combinations of DNA-encoded antigens and/or cytokines may be administered; (i.v.) genetic stability; (v) potential speed of making new vaccines with genetic identity; (vi) development of vaccines for agents that cannot be grown in culture; (vii) no need for a cold chain; and (viii) possibility of modulation of the immune response. The perceived risks include: (i) integration of the plasmid into the host genome; (ii) induction of anti-DNA antibodies and autoimmunity; and (iii) induction of tolerance. The available information concerning safety is encouraging, with the risk of integration being considered to be orders of magnitude below the spontaneous mutation frequency in humans. DNA immunization offers the possibility of extending the control of infectious diseases far beyond those that are currently controlled by conventional and recombinant vaccines, to include vaccines for parasites and cancer. However, it is currently too early to predict the future extent of use of **DNA vaccines** in human immunization programs because the initial clin. trials are still in progress.

L15 ANSWER 13 OF 14 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:204105 BIOSIS
DOCUMENT NUMBER: PREV199900204105
TITLE: Improved immunogenicity of HIV-1 epitopes in HBsAg chimeric DNA vaccine plasmids by structural mutations of HBsAg.
AUTHOR(S): Bryder, Karin; Sbai, Hakima; Nielsen, Henrik V.; Corbet, Sylvie; Nielsen, Claus; Whalen, Robert G.; Fomsgaard, Anders [Reprint author]
CORPORATE SOURCE: Molecular Biology Laboratory, Department of Virology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S, Denmark
SOURCE: DNA and Cell Biology, (March, 1999) Vol. 18, No. 3, pp. 219-225. print.
CODEN: DCEBE8. ISSN: 1044-5498.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 May 1999
Last Updated on STN: 26 May 1999

AB To improve the immunogenicity of epitopes from the envelope protein of HIV-1, we have developed **gene gun**-delivered subunit DNA vaccines by inserting the sequences encoding the V3 region into the hepatitis B virus (**HBV**) envelope **gene**, often called the surface antigen (HBsAg). We have examined the possibility of modifying the immune response to V3 by introducing modifications into the carrier HBsAg in **gene gun** DNA immunization of mice. In some plasmid constructions, the V3 sequence was introduced into the preS2 region of the HBsAg. Although this region is not present in all protein subunits of the HBsAg particles produced, abolishing the internal translational initiation site for the S protein had no effect on the immune response to V3. Expression of V3 at the N-terminal or C-terminal part of the HBsAg protein resulted in equal anti-V3 antibody and cytotoxic T-lymphocyte (CTL) responses. However, elimination of secretion by single amino-acid mutations in the HBsAg decreased the anti-HBsAg antibody response but enhanced the anti-V3 antibody response. In contrast, the CTL response to V3 was independent of the structural mutations but could be improved by a total deletion of the HBsAg sequence part. Thus, the immune response to heterologous epitopes can be altered by modifications in the carrier HBsAg protein. Modifications of the HBsAg carrier might interfere with the dominant immune response to the HBsAg epitopes, allowing better antibody induction to less immunogenic foreign epitopes. However, for induction of CTL responses, the expression of minimal epitopes may be advantageous.